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I was asked to find a way to further solubilize CoQ10 than the ~5% that theoretically could be obtained in soybean oil, and to use some kind of co-solvent if needed. My first guess was to solubilize it in D-Limonene, because it acts like a total solvent with beeswax — you need ≥10% beeswax in formulations that have a high limonene content because it just dissolves the beeswax but it wasn't there. So I took 50g of D-Limonene and started stirring in CoQ10, one or two grams at a time, by hand, and at room temperature. I stopped at 40% CoQ10 (20 grams in 50g D-Limonene), although I could have dissolved more in there. After about 30% or so, the solution starts to get a little cloudy after adding the CoQ10, but with 1-3 minutes of steady, slow stirring with the glass rod the CoQ10 completely dissolves and the solution clears up. After getting a clear, dark red 40% solution of CoQ10 in D-Limonene, I wanted to see what would happen when the solution was added to oil, since pure D-Limonene isn't really practical for a softgel fill — although we do make such a product. I added the CoQ10/D-Limonene solution to 50g of soybean oil — 1 or 2 g at a time — until I ended up adding the entire amount of CoQ10 solution to the soybean oil. It resulted in a clear, dark red solution, with no precipitation or phase separation at all — we'll see how it is after some time passes, although I don't expect anything bad to occur at all. The final soybean oil/D-Limonene/CoQ10 overall is 20% of CoQ10 that is completely solubilized.

3/17

The 20% CoQ10 in 50:50 Soy/Limonene shows ~1-2% precipitation out over the weekend (~1 gram).

The trial that I added 10% D-Limonene shows the same amount of 2 powder at the bottom as on Friday, which is mostly or all D-Limonene.

The one to 10% glycerol still has the glycerol at the bottom, separated, but no other precipitate is evident.

The one to 10% vitamin E shows a dark (amber-brown) when I first added it, which it still is, but no precipitation.

The one I added 10% water to precipitated a very small amount at the interface.

The one to 10% lecithin shows no separation or precipitation.

Next I am going to try and make a solubilized CoQ10 in limonene solution and then combine it into some CoQ10 formulations with soybean oil.

Witnessed &amp; Understood by me,

Date

Invented by

Date

Recorded by

3/14/83

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From Page No. 144 Any beeswax and see how it comes out and how it behaves after some time passes. The formula for CC-930 (CoQ10 100mg) is:

Co-FA-MX-00016	Cocoyne <u>Q10</u>	104.0900mg	100grams
VI-FA-MX-00191	4-SO med Tocopherols 322mg	269.0300mg	1.45g
RE-FF-MX-00077	Rice Bran Oil	176.0200mg	.35g
BE-PA-MX-00053	Yellow Beeswax	20.0000mg	10.52g
BE-FA-MX-00203	Natural Beta Carotene 255,820mg	10.0500mg	3.45g
		580.0000mg	1.73g

I'm going to try, first of all, to remove the Beeswax and the Rice Bran Oil and dissolving the CoQ10 in the same amount of Limonene that would be the weight of the RBO and beeswax, together (196.0200 mg/eq), so there'll be enough to dissolve it, then add the Vitamin E & Beta Carotene. Hopefully, the Vitamin E will help to keep the CoQ10 dissolved. Also the trial is the smell and I did on Friday maybe I'll keep the Beta Carotene out of the formula so I can see it for a few days - then add it. Anyway, here is the formula I will use:

Cocoyne <u>Q10</u>	104.0900mg	100grams
4-SO med Tocopherols	269.0300mg	1.45g
D-Limonene	196.0200mg	46.35g
Natural Beta Carotene	10.0500mg	33.97g
	580.0000mg	1.73g

The Limonene should not degrade the CoQ10, as the Limonene is a solvent and for CoQ10 CC1=C(C(=O)O)C=CC(=C)C1 - there is nothing there that will react with Limonene, so there should be no problem - the Limonene is just acting as an organic solvent - nothing more, nothing less.

Wow! As soon as you add the Vitamin E to it (and it's very light-colored Vitamin E) it turns a dark purple color! I hope it's just due to a change in oxidation state of one or both the Vitamin E and CoQ10 - there isn't anything that should react to change the structure of anything there. Made some CoQ10 (but this same amt as Vit E in the other one) - no discoloration. It looks good, but I'm having assays done to see if anything happened.

Actually, looking at it, I'm not sure I should tell what To Page No. 146

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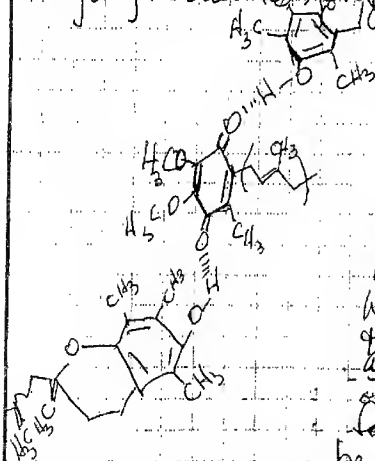
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happened. The fully oxidized ketone groups on the quinone moiety of the Colloidal oxidized the hydroxyl group of the chromenol on the D-α-tocopherol, becoming a semi-quinone. Since the Colloidal is fully solubilized and the two molecules are in a compatible solvent, this would happen easily. There is nothing in any of the three molecules that could do anything else (no bonds broken, no ~~acid~~ <sup>acid</sup> ~~hydroxyl~~ <sup>hydroxyl</sup> ~~alkylation~~ <sup>alkylation</sup> happening, or anything) — there has just been a change in the oxidation states and the solution absorbs light at a different wavelength, that's all — in fact, it would make both molecules more like their active states, anyway. A similar thing happens to the Shalee Colloidal product in the gelatin — it darkens from an orange color to a deep brick red as the Colloidal becomes more solubilized and reacts with the Vitamin E in the product. It doesn't gel as easily as the because 1) there isn't as much Vitamin E in the Shalee product, and 2) the Colloidal doesn't solubilize as much in the Shalee product — both things happen here, and all the constituents are just as active as they should be.

The mixture that I made last night with less than in the place of the Vitamin E looked real good last night, but was very precipitated today — no good. I'm really encouraged with this project, though.

Thinking more on the interaction between the Colloidal and Vitamin E, it may only be due to hydrogen bonding between the molecules, like this:



Even if the two molecules were, in fact, causing partial oxidation state changes in each other, or if they were hydrogen bonding, either one is fine as far as their function and activity goes, and the only real change in them is not structural, or functional, so I don't see any problem here, other than maybe having to convince some of the less technical ones here about what, in fact, is happening and that the color change is nothing to worry about. Actually, if they are just changing the oxidation state of each other, that's all towards the more functional form of both molecules. For Chemical help — I'd be enormously surprised if it were anything else. I don't think anything is possible.

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3/1/03

TITLE

College Scholarship

3/21/03

I can't think of any other reason for this happening.  
As for the assay I requested on the mix I made that was comparable to our CC-930 100mg CoQ Sol. ~~then~~ they came out well - the CoQ 10 was 110% of claim and the Vitamin E (mixed tocopherols) came out with good results for the separate components; in fact the gamma-tocopherol peak was as high as the D-alpha peak for our Chem 4-50 Vitamin E. There were no unexpected peaks in either assay, so it gives my claim that the Inmune doesn't hurt any of the substances and that the color change that occurs after adding the vitamin E to the solubilized CoQ 10 is not due to anything other than a change in oxidation state. I'm very encouraged by all this, and am waiting to hear exactly what they want me to do with it - there's a lot of possibilities ~~for~~ here, if we do it right.

3/26/03

3/26/03  
Now I'm told to go ahead and try solubilizing 28-30% Colno in toluene, but they want me to add سورفونر or something to it — just don't like the idea of so much money, although I'd won't trust anything else I made up before — off the 100% Col Sol product — the one that tested out so well, ended up with a small amount of crystals that formed on the bottom of the vial over time, so I'm convinced & lost of 33% B, just too much for it — but adding all that much

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3/19/05

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15. Vitamin E - or anything else increases the chance that the Colloidal will precipitate out - the one with 33% Colloidal in Linnene and only 10% Vitamin E added, back on 3/14 still shows no precipitation, so that's encouraging, but I really don't think we need to add anything else, just the Colloidal in Linnene - the Linnene won't hurt anything and it's already grand tailored in as a safe nutritional supplement to the diet, so there's no regulatory problems with it.

End

TITLE TK-69

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Sample of  
Linnene is the

AS-FA-MX-1  
VI-FA-MX-1  
VI-FA-MX-0  
VB-FA-MX-1  
VB-FA-MX-0  
NI-FA-MX-1  
NI-FA-MX-1  
VB-FA-MX-1  
FO-FA-MX-1  
VB-FA-MX-1  
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CA-FA-MX-1  
PA-FA-MX-1  
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SE-FA-MX-1  
CH-FA-MX-1  
IN-FA-MX-1  
HO-FA-MX-1  
CO-FA-MX-1  
SA-PA-EX-1  
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